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EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,643	CASTAN ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-11 and 13-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-11 and 13-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 October 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/25/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

NEW REJECTIONS

Drawings

The drawings are objected to because the axis labels and legends are not in English. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

MAINTAINED REJECTIONS

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17-19, and 24-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-17 and 19-31 of copending Application No. 10/522,252 in view of Carvais. Both the instant application and application 10/522,252 teach an oral suspension of a drug (both teach many of the same classes and particular drugs, including naproxen, ganciclovir, and morphine) containing microcapsules coated at 1% to 50% (by mass) with a film comprising a film forming polymer insoluble in gastrointestinal tract fluid, a nitrogen containing polymer, a

plasticizer, and a surfactant/lubricant. Both also teach that the microcapsules are less then 1000 μm in size. Application 10/522,252 does not teach that the liquid phase of the suspension is saturated with the drug. Carvais teaches a suspension of drug that contains microcapsules of the drug, present at about 5%, and whose liquid phase is saturated with the drug. One of ordinary skill in the art at the time the invention was made would have found it obvious to use the teachings of Carvais to modify the invention of application 10/522,252 to practice the instant invention to have a product capable of instant as well as prolonged drug delivery.

Claims 1-3, 5, 7-10, 17, 19, and 24-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9, 11-24, 26, 31, 41-50, 58-76, 89-91, 99-101, and 113 of copending Application No. 11/707,034 in view of Carvais. Both the instant application and application 11/707,034 teach an oral suspension of a drug containing microcapsules coated with a film comprising a film forming polymer insoluble in gastrointestinal tract fluid, a nitrogen containing polymer, a plasticizer, and a surfactant and/or a lubricant. Both also teach that the microcapsules are less then 1000 μm as well as the inclusion of anti-viral drugs. Application 11/707,034 does not teach that the liquid phase of the suspension is saturated with the same drug contained in the microcapsules. Carvais teaches an oral suspension of drug that contains microcapsules of the drug and whose liquid phase is saturated with the drug. One of ordinary skill in the art at the time the invention was made would have found it obvious to use the teachings of Carvais to modify the

invention of application 10/707,034 to practice the instant invention in order to have a product capable of instant as well as prolonged drug delivery.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7-11, 17-19, and 21-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carvais (previously cited) in view of Autant et al. (previously cited).

Carvais teaches a sustained release liquid oral suspension that comprises a suspension with microcapsules of a drug suspended in a saturated solution of the drug, where dissolution of the microcapsules maintains the saturation level of drug in solution (see column 1 lines 26-38; instant claims 1, 5, 7-8, and 19). Dissolution of the microcapsules over time as drug is removed from the liquid brings the concentration in the liquid back to the level of saturation (instant claims 5 and 23). This liquid phase is taught to be either non-aqueous or aqueous (see column 1 lines 18-19 and 21-23). Carvais also teaches that the invention is suitable for drugs that run the spectrum from water insoluble to water soluble (see column 1 lines 16-25). In one embodiment, Carvais teaches that 158.33 mg of drug is suspended in 5 ml of water vehicle which translates to about 3% microcapsules and 97% vehicle (see example I). Carvais teaches that this amount of drug in suspended form can be adjusted upward (see example I; instant claims 21-22). A subsequent example does just this where approximately 5% microcapsules is in about 95% vehicle (see example III; instant claims 4 and 21-22). While, Carvais teaches the microcapsules to be encapsulated drug, beyond the drug to be included, Carvais does not teach a particular microcapsule composition.

Autant et al. teach a set of coated particles (microcapsules) that contain any number of active principle components (drugs) (see abstract). In particular, the coating is taught to be composed of the following components:

1. "at least one film-forming polymer (PI) which is insoluble in the liquids of the digestive tract, present in a quantity of 50 to 90%, preferably 50 to 80% by weight of dry matter of the whole coating composition, and consisting of at least one non-hydrosoluble cellulose derivate, ethylcellulose and/or cellulose acetate being preferred;

2. at least one nitrogen-containing polymer (P2), present in a quantity of 2 to 25, preferably 5 to 15% by weight of dry matter of the whole coating composition, and consisting of at least one polyacrylamide and/or one poly-N-vinylaride and/or one poly-N-vinyl-lactam, the polyacrylamide and/or the polyvinylpyrrolidone being preferred;

3. at least one plasticizer present in a quantity of 2 to 20%, preferably 4 to 15% by weight of dry matter of the whole coating composition, and consisting of at least one of the following compounds: glycerol esters, phthalates, citrates, sebacates, cetylalcohol esters, castor oil and cutin, castor oil being particularly preferred;

4. at least one surface-active and/or lubricating agent, present in a quantity of 2 to 20%, preferably 4 to 15% by weight of dry matter of the whole coating composition, and chosen from anionic surfactants, preferably the alkali metal or alkaline-earth metal salts of fatty acids, stearic acid and/or oleic acid being preferred, and/or from nonionic surfactants, preferably polyoxyethylenated esters of sorbitan and/or polyoxyethylenated esters of sorbitan and/or polyoxyethylenated derivatives of castor oil, and/or from lubricants such as stearates, preferably calcium, magnesium, aluminum or zinc stearate, or such as stearylfumarate, preferably sodium stearylfumarate, and/or glyceryl behenate,

said agent comprising only one or a mixture of the above products" (see column 6 line 55-column 7 line 32; instant claims 1 and 2).

A particular coating embodiment combines ethyl cellulose, poly(vinyl pyrrolidone), castor oil and magnesium stearate (see column 16 lines 38-48; instant claim 2). The particles are taught to have a size of "between 50 and 1000 microns, preferably of between 100 and 750 microns and, more preferably, of between 100 and 500 microns" (see column 7 lines 33-35; instant claims 9 and 24-25). Autant et al. go on to teach that the coating constitutes 5 to 40% by weight of the particles and is applied in a single layer (see column 11 lines 59-61 and column 12 lines 12-13; instant claims 3, 10, and 26). A listing of active principle compounds that are envisioned within the particles are taught by Autant and all of these compounds are also claimed by applicant (see column 10 lines 55-65; instant claims 17-18).

The only detail provided by Carvais about the components in the microcapsules in the taught suspension is the presence of drug. Since sustained release of drug is a main goal of the Carvais invention, it would have been obvious to one of ordinary skill in the art at the time the invention to include microcapsules in the saturated suspension that provide sustained release of the contained drug to facilitate this desired property. When considering the possible configurations of microcapsules to include in the composition of Carvais, three basic configuration options exist: 1) coated microcapsules, 2) uncoated microcapsules and 3) a collection of both coated and uncoated microcapsules. The use of any of these configurations of sustained release microcapsules in the invention of Carvais would have been expected to result in a sustained release composition as taught by Carvais. As a known microcapsule drug

preparation that provides sustained release of the drug, it would have been obvious to one of ordinary skill in the art to employ the coated particles of Autant et al. as the microcapsules in the sustained release, drug saturated suspension of Carvais. This would then address two of the three configuration options, the first where only the coated particles of Autant et al. are used as the microcapsules in Carvais and the second where the coated particles of Autant et al. are included with uncoated particles. In addition, since the combined references teach embodiments with the same drug and coating, as well as the same proportions of drug, coating components and coated particles as that taught by the applicant, absent any evidence to the contrary, the release profile claimed by the applicant would necessarily be present in the invention of the Carvais in view of Autant et al. (see instant specification example 2; instant claim 1). According to MPEP 2112.01, "A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present." This treatment results from In re Spada, which states that, "Products of identical chemical composition can not have mutually exclusive properties." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Thus, the limitations of claims 1, 11, and 27 are also taught by Carvais in view of Autant et al. Therefore, claims 1-5, 7-11, 17-19, and 21-27 are obvious over Carvais in view of Autant et al.

Claims 1-2, and 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carvais in view of Autant et al. as applied to claims 1-5, 7-11, 17-19, and 21-27 above, and further in view of Turck et al. (US Patent No. 6,184,220).

Carvais in view of Autant et al. makes obvious an aqueous suspension saturated with drug and containing either coated drug particles or both coated and uncoated drug particles, where the coating contains the claimed constituents. This modified reference does not explicitly teach particular components other than water in the liquid vehicle (see instant claims 1-2).

Turck et al. teach a liquid drug suspension where many of the drugs are also claimed in the instant claims (see abstract and column 5 lines 16-20). Turck et al. teach a liquid medium for this suspension whose pH is between 2 and 4 that comprises buffering agents (solubility modifier), sweetener, glycerol (rheology modifier), and water soluble cellulose polymer (rheology modifier) (see column 8 lines 26-36 and 42-46; instant claims 13-16). It would therefore have been obvious to one of ordinary skill in the art at the time the invention was made to induce an acidic pH and include a solubility modifier, rheology modifier or sweetener in the aqueous vehicle of Carvais in view of Autant et al. since these were known components and properties used in oral liquid dispersion media (variations that would have been predictable to one of ordinary skill in the art). Therefore claims 1-2 and 13-16 are obvious over Carvais in view of Autant et al. and Turck et al.

Claims 1 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carvais in view of Autant et al. as applied to claims 1-5, 7-11, 17-19, and 21-27 above, and further in view of Ulrich et al. (previously cited).

Carvais in view of Autant et al. makes obvious an aqueous suspension saturated with drug and containing either coated drug particles or both coated and uncoated drug particles, where the coating contains the claimed constituents. This modified reference does not explicitly teach a kit configuration for the suspension components (see instant claims 1-2).

Ulrich et al. teach a suspension of coated drug particles (see abstract). Ulrich teach that a dry powder form of the coated drug can be provided for later reconstitution with a liquid vehicle (kit) (see paragraph 34 line 7-9; instant claim 20). As a known means of improving a similar composition (e.g. composition configuration for end use), it would have been obvious to one of ordinary skill in the art at the time of the invention to configure the suspension components of Carvais in view of Autant et al. as a dry preparation of coated and uncoated particles and a separate liquid vehicle. The proportions of the uncoated and coated particles would have been obvious to one of ordinary skill in the art so as to produce a saturated liquid vehicle with suspended coated particles. Thus, claims 1 and 20 are obvious over Carvais in view of Autant et al. and Ulrich et al.

Response to Arguments

Applicant's arguments filed September 25, 2009 have been fully considered but they are not persuasive.

Rejections under 35 USC 103 (a):

The affidavit filed September 25, 2009 is acknowledged.

Rejections under 35 USC 103 (a):

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Specific arguments directed against the teachings of Ulrich et al. focus on the formulation of the suspended microparticles taught by this reference. This reference was cited to demonstrate what was known in the prior art regarding how liquid oral pharmaceutical suspensions were configured for distribution to pharmacists and ultimately their end-user. Thus, the Ulrich et al. reference was cited for the background information it provides as to the state or the prior art. When determining whether a claim is obvious, an Examiner must make "a searching comparison of the claimed invention – including all its limitations – with the teaching of the prior art." *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995). Thus, "obviousness requires a suggestion of all

limitations in a claim." *CFMT, Inc. v. Yieldup Int'l. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)). Furthermore, as the Supreme Court recently stated, "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). The Ulrich et al. reference provides this required rationale because it provides evidence of what was known in the prior art, as stated in the Office Action mailed May 25, 2009.

Applicants also argue the level of ordinary skill in the art was not resolved and that the Graham factors were not addressed. The Graham factors were considered and addressed. Moreover, the resolution of the level of ordinary skill in the art need not be explicit (see MPEP 2141 II C).

Applicants further argue that one of ordinary skill in the art would not have expected that the combination of Carvais and Autant et al., would yield a composition where the coating structure would remain unchanged and provide a similar release profile on day ten compared to day zero. According to MPEP 2144, "The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant." Therefore, the ordinarily skilled artisan need not anticipate the result applicants purport in order to combine the cited references and find obvious the collection of components that constitute applicants' composition.

While applicants correctly note that unexpected results must be weighed against the evidence supporting an obviousness rejection, applicants' "unexpected results" were not gleaned as a result of comparison to the closest prior art as required (see MPEP 716.02(e)). In addition, applicants also have not established the statistical and practical significance of the supposed unexpected result. Therefore, the "unexpected results' touted by applicants are not sufficient to overcome the finding of obviousness.

Provisional Nonstatutory-type obviousness rejections:

Applicants argue that the provisional double patenting rejections are in err because the filing date of the conflicting copending applicants are after that of the instant application. This is not found persuasive because MPEP 804 I B states that the application of provisional double patenting rejections between two copending applications is appropriate.

Further arguments regarding copending application 10/522252 cite the purported "unexpected results" as a reason for the nonobviousness of the instant invention over the subject matter claimed in this copending application. Applicants' unexpected results were addressed above and that response is reiterated here.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615